REMARKS

Claims 1-8 and 11-17 are pending in the application. Claims 1-8 have been cancelled by this amendment. New claims 20-23 have been added to the application. Therefore, claims 11-17 and 20-23 are at issue.

This amendment is submitted in accordance with 37 C.F.R. §1.116(a) and §1.116(b) in order to present the rejected claims in a better form for allowance or appeal. The amendment is necessary to eliminate a rejection under 35 U.S.C. §103. This amendment was not presented earlier because applicants believed and still believe that the amendment mailed February 6, 2003 overcame the rejection under 35 U.S.C. §103. The amendment should be entered because (a) it places the application in better form for allowance or appeal, and the amendment does not require further searching or present any new issues, and (b) a Request for Continued Examination (RCE) is submitted concurrently with this amendment.

The courteous telephonic interview granted to applicants' undersigned attorney by Examiner Cook on August 26, 2003 is hereby acknowledged with appreciation. During the interview, the outstanding Office Action, cited reference, and claims on file were discussed in detail.

New claims 20-23 have been added to the application. These new claims are fully supported in the application as originally filed, see, for example, original, and now-cancelled, claim 4 and claim 16, and

the specification at page 7, lines 26-28, and page 9, line 32 through page 10, line 3.

Claims 1-8 and 11-17 stand rejected under 35 U.S.C. §103 as being obvious over Daugan U.S. Patent No. 6,140,329 ('329). This rejection is based on the contention that the '329 patent discloses the compound recited in the claims, use of the compound to treat sexual dysfunction, oral administration, and a dosage encompassing the recited dosage range. In view of the unexpected results demonstrated by the claimed compound at the claimed low dosage (i.e., about 1 to about 20 mg) and claimed low maximum total daily dose (i.e., maximum 20 mg/day), it is submitted that this rejection is in error and should be withdrawn.

In particular, composition claims 1-8 have been cancelled without prejudice. In view of the telephonic interview, these composition claims have been cancelled to facilitate prosecution, and not because of questions relating to patentability. The composition claims will be pursued in a continuation application.

It is submitted that for the reasons set forth in Amendment "A" mailed February 6, 2003 and incorporated herein by reference, and because of the new and unexpected results achieved by the present invention, it is submitted that method claims 11-17 and new claims 20-23 would not have been obvious to a person skilled in the art, and the rejection of the pending claims under 35 U.S.C. §103 over the '329 patent should be withdrawn.

The present claims recite a method of treating sexual dysfunction in a patient in need thereof by

the oral administration of a unit dosage composition containing about 1 to about 20 mg of a specifically claimed compound, up to a maximum dose of 20 mg per day. The method can be used to treat sexual dysfunction, including, for example, male erectile dysfunction (MED) and female arousal disorder (FAD), as recited in the claims. As discussed in Amendment "A" and hereafter, the cited reference fails to teach or suggest a method of treating sexual dysfunction using about 1 to about 20 mg of the claimed PDE5 inhibitor, up to a maximum total dose of about 20 mg per day.

It is submitted that the examiner's obviousness conclusion is incorrect because the '329 patent fails to teach or suggest a low oral dosage of the claimed PDE5 inhibitor to effectively treat sexual dysfunction. In addition, the presently claimed invention provides unexpected benefits and is a substantial advance in the art. In particular, the presently claimed invention (a) effectively treats sexual dysfunction using a low dose of a particular PDE5 inhibitor, (b) eliminates or reduces various adverse side effects associated with current PDE5 inhibitor therapy used to treat sexual dysfunction, i.e., VIAGRA®, and (c) increases the population treatable for sexual dysfunction using a PDE5 inhibitor.

In particular, the '329 patent discloses a class of PDE inhibitors, including the compound recited in claim 13, useful in oral dosage forms over a range of 0.2-400 mg to treat sexual dysfunction. However, all examples in the '329 patent teach using 50 mg of active compound per dosage form. See columns 8-10 of

the '329 patent. The '329 patent provides no teaching or suggestion of a preferred unit dose, except for the 50 mg dose in the examples. Thus, the lowest dose of PDE5 inhibitor embodied in the '329 patent in a unit dose composition is 50 mg of the active ingredient.

Although column 10, lines 1-3 of the '329 patent states that "other doses may be prepared," this teaching does not address the dosage needed for an effective treatment of sexual dysfunction. This statement in the '329 patent merely is directed to teaching those skilled in the art how to make a different unit dose. This teaching of the '329 patent, however, fails to instruct whether the 50 mg dose should be increase or decreased.

Therefore, although the '329 patent teaches a unit dosage range for the disclosed compounds of 0.2 to 400 mg, administered once or several times per day, the '329 patent does not teach or suggest a low *maximum* daily dose for effective treatment of sexual dysfunction. An important feature of the present invention is administration of an oral dose of the claimed unit dosage composition at 20 mg or less, per day, to treat sexual dysfunction (see claim 13). Such a feature is neither taught nor suggested in the '329 patent.

The '329 patent discloses thirteen specific compounds, and two preferred compounds, for the treatment of impotence. One of the preferred com-pounds, i.e., Example 1 (Compound A) of the '329 patent is Compound (I) recited in the present claims.

Even though Compound (I) is disclosed as a *preferred* compound, the '329 patent contains no teach-

ing or suggestion that Compound (I) can be expected to successfully perform at a dosage less than 50 mg. The '329 patent merely teaches a broad dosage range for a class of compounds and for particular individual compounds. The only specific dosage disclosed in the '329 patent, and particularly for Compound (I), is 50 mg.

Accordingly, insofar as the '329 patent does not disclose any dose below 50 mg for Compound (I) or any other compound, the '329 patent can be read to teach that a 50 mg dose is an effective dose of Compound (I). The disclosure at column 10, lines 1-3 of the '329 patent does not alter this teaching for the reasons set forth above. The lack of an example or any specific disclosure relating to a lower dose (i.e., less than 50 mg) for the *preferred* compounds of the '329 patent implies that it was not understood a lower dose of the claimed compound could effectively treat sexual dysfunction.

The '329 patent contains *no* disclosure that would lead a person skilled in the art to consider using the presently claimed low unit dose and maximum daily dose of Compound (I) with any reasonable expectation of successfully treating sexual dysfunction. In contrast, the present claims are enabled and supported by the clinical trials set forth in the specification. The specification, in Examples 6 and 7, clearly shows that a low dose of Compound (I) successfully treats sexual dysfunction *and* leads to a reduction or elimination of various adverse side effects.

In summary, there is no basis to contend that the presently claimed unit dosage composition or method

would have been obvious from the '329 patent, which merely teaches a broad dosage range for a class of PDE5 inhibitors to treat sexual dysfunction. Furthermore, there is no incentive to provide a claimed unit dosage composition based on the examples of the '329 patent (limited to 50 mg dose).

The examiner states that no unexpected results are demonstrated for the claimed enantiomer. To the contrary, as discussed in Amendment "A" at pages 7-9, and incorporated herein by reference, the claimed enantiomer possesses improved properties over its three stereoisomers.

In addition, the presently claimed invention satisfies a long-felt need in the art. A unit dosage composition containing Compound (I) is in the final approval stages at the Food and Drug Administration. After approval, which is expected in late 2003, the unit dosage form containing Compound (I), also known as tadalafil, will be marketed under the tradename CIALIS®. CIALIS® will be in direct competition with VIAGRA®. CIALIS® (i.e., a unit dosage composition of the present invention) overcomes some of the disadvantages associated with prior PDE5 inhibitor treatments of sexual dysfunction, e.g., VIAGRA®, and provides an unexpected improvement in the art.

Applicants have discovered that the compound recited in independent claim 13 can be administered in a unit dosage composition containing about 1 to about 20 mg of the compound, up to a maximum dose of 20 mg/day, to provide an effective method of treating sexual dysfunction, while reducing or eliminating

various adverse side effects associated with VIAGRA®. This aspect of the present invention is discussed in Amendment "A," pages 11-14, incorporated herein by reference.

For example, clinical studies have shown that a method of treating sexual dysfunction utilizing a presently claimed unit dosage effectively reduces flushing or visual abnormalities in susceptible individuals. See Examples 5-7, at pages 26-30 of the specification, wherein administration of the claimed unit dosage composition reported incidence of flushing below 2%. This incidence rate of flushing demonstrates marked improvement over VIAGRA®, i.e., 10% flushing incidence rate reported on the VIAGRA® label.

A person skilled in the art would not have been motivated from the '329 patent to provide a method as recited in the present claims with any expectation that claimed unit dosage and low maximum daily dose would provide such unexpected results in the treatment of sexual dysfunction. From a reading of the '329 patent, it would have been expected that a dose *greater* than a daily 20 mg maximum dose of Compound (I) is needed to treat sexual dysfunction effectively, i.e., about 50 mg. Additional unexpected benefits of the present invention are the improvements demonstrated by the claimed over present-day, commercially available PDE5 inhibitor treatment for sexual dysfunction. The present invention, therefore, not only is nonobvious over the '329 patent, but also satisfies long-felt and unmet needs in the art.

In summary, the presently claimed invention would not have been obvious over the '329 patent, and the invention satisfies a long-felt need in the art. All examples in the '329 patent teach a 50 mg dose of the active compound. The cited art absolutely fails to suggest that a low dose of any PDE5 inhibitor, let alone the specific PDE5 inhibitor recited in claim 13, can be used in a method to successfully treat sexual dysfunction, while eliminating or reducing various adverse side effects associated with the current PDE5 inhibitor treatment for sexual dysfunction.

Applicants, therefore, have discovered a method of treating sexual dysfunction wherein a particular *low* unit dosage composition containing a particular PDE5 inhibitor effectively treats sexual dysfunction using a 20 mg/day maximum dose, while avoiding or reducing various adverse side effects. The '329 patent broadly discloses a dosage range for various PDE5 inhibitors, but fails to teach or suggest the specific unit dosage, maximum daily dosage, *and* the specific compound of the present invention that provides such new and unexpected benefits.

It is submitted, therefore, that the claims are now in proper form and scope for allowance. An early and favorable action on the merits is respectfully requested.

Should the examiner wish to discuss the foregoing, or any matter of form in an effort to advance this application toward allowance, the examiner is urged to telephone the undersigned at the indicated number.

Respectfully submitted,

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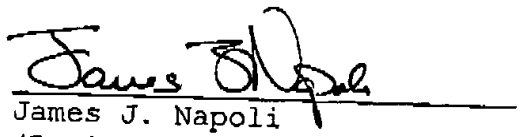
By 

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